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The impact of childhood cancer on parental separation, divorce and family planning in Denmark

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Conflict of interest

No conflicts of interest to declare.

Contributors´ statement

LM and FE are the principal investigators, conceptualized the study, contributed to the data collection, data analyses and interpretation, and manuscript preparation, editing, and review. TTN and AK contributed to the acquisition and preparation of data. MH, LEF, PEB, SKK, SOD, and JFW contributed to the data interpretation, critically reviewed and revised the manuscript.

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Precis

Having a child with cancer was not associated with an overall adverse impact on parents' risk of separation or divorce and future family planning. These encouraging findings should be communicated to parents to support them along their child´s cancer trajectory.

Abstract

Background: Childhood cancer is a devastating experience for the family. We aimed to assess the impact of having a child with cancer on parental separation, divorce, and future family planning in Denmark.

Methods: We conducted a nationwide cohort study using Danish registry data. Parents of children diagnosed with cancer in 1982-2014 (n=7066 children, n=12418 case parents) were matched with ten comparison parents of cancer-free children (n=69993 children, n=125014 comparison parents). We used discrete-time Cox regression models to compare the risk of separation (end of cohabitation) and divorce between case and comparison parents, and to identify risk factors of separation and divorce among case parents only. Descriptive statistics were used to compare family planning between case and comparison parents.

Results: Case parents had a slightly lower risk of separation (HR=0.96, 95%-CI: 0.93-0.99) and divorce (HR=0.92, 95%-CI: 0.87-0.97) than comparison parents. We found that case parents aged <45 years, with short education, and who were unemployed were at increased risk of separation and divorce. Moreover, parents of children diagnosed with cancer at a young age (aged <15 years) were more likely to separate or divorce. We observed no differences in the total number of children and time to next child after the cancer diagnosis between case and comparison parents.

Conclusions: Having a child with cancer was not associated with an overall adverse impact on parents' risk of separation or divorce and future family planning. These encouraging findings should be communicated to parents to support them along their child´s cancer trajectory.

Keywords

childhood cancer; parents; separation; divorce: family; registry; cohort

Introduction

Childhood cancer is a devastating experience and may affect the psycho-social functioning of all family members[1]. Having a child with cancer may disrupt families´ daily routine for long time periods and requires adaptation of family structures and changes in parental responsibilities to accommodate the needs of the sick child[2]. The parents are suddenly confronted with the risk that their child may die and the risk of severe side and late effects of treatment. Feelings of fear and uncertainty together with high caregiving demands may predispose parents to emotional stress reactions after the child´s diagnosis[3]. Increased caregiving and practical demands together with the psychological burden of having a child with cancer may strain the parental relationship and contribute to family conflicts[4]. Moreover, during the child's treatment, parents are often physically separated with one parent spending time in the hospital and the other parent staying at home with the child's siblings or meeting work-related obligations[5].

Understanding the impact of childhood cancer on the parental relationship and future family planning is crucial to develop adequate guidance along the child´s cancer trajectory. To date, only few studies have assessed the impact of childhood cancer on the parental relationship by using a quantitative approach; none of which observed increased risks for divorce or separation among parents of children with cancer[6-8]. One study was of cross-sectional design[8] and the other two studies were of longitudinal character, but included parents of children diagnosed up to 1997[6] and 2001[7] reflecting the situation of 20 years ago. However, patterns of divorce or separation among parents of children with cancer may have changed due to general societal changes, improvements in treatment modalities for childhood cancer, considerably increased survival[9], and lower risks of late effects[10]. Evidence related to the impact on future family planning is entirely lacking. Based on the childhood cancer experience and the related parental burden, we expect parents having a child with cancer to have fewer children compared to parents of cancer-free children or to postpone having another child after the diagnosis. The high-quality Danish registers provide unique opportunities to address these research questions prospectively due to the availability of detailed information with virtually no loss

to follow-up. We initiated a nationwide cohort study in Denmark to assess the impact of childhood cancer on parental separation, divorce, and future family planning in Denmark.

Methods

Design and research setting

We conducted a nationwide population-based cohort study based on Danish registry data. Denmark has a civil registration system based on unique personal identification numbers (PIN) and various nationwide administrative registries including the Danish Cancer Registry[11], the Central Population Register[12], Statistics Denmark[13], and the Medical Birth Register[14]. The PIN is used in all registries, enabling accurate linkage of individual information across registries[13].

Study population

The study population has been previously described[15] and further information is provided as Supplementary Material. Briefly, we identified 7636 children diagnosed with cancer before the age of 20 years in 1982-2014 from the Danish Cancer Registry[11] (Figure 1). The children´s PIN allowed linkage to their parents via the Civil Registration System[12] and Medical Birth Register[14]. Children were excluded if parental information was lacking, no parent was living with the child at the time of diagnosis, or if either of the parents had other children diagnosed with cancer before 1982. We applied a matched cohort design to compare parents of children with cancer (*case parents*) to parents of cancer-free children (*comparison parents*). Ten comparison parents per case parent were randomly sampled (sampling with replacement) from the entire population of Denmark, individually matched by child´s year of birth and parental decade of birth. Among case and comparison parents, we excluded parents and children with Down syndrome and parents aged <15 years at birth. The final study cohort included 12418 case parents (n=6833 mothers, n=5585 fathers) and 125014 comparison parents (n=68773 mothers, n=56241 fathers).

Separation, divorce, family planning

Information on separation, divorce, number of children and children´s date of birth was obtained from the Danish Civil Registration System[12] and the Medical Birth Registry[14]. Separation was defined as parents no longer living at the same address to account for the increasing number of couples

cohabiting without being married[16]. For the analyses of family planning, we calculated the total number of children other than the index child (child with cancer/reference child), the number of children before the index date (date of diagnosis/reference date), and the number of children after the index date. Time to birth of next child was defined as the number of days between the index date and the date of birth of the first child thereafter.

Socio-demographic and cancer-related characteristics

Socio-demographic characteristics of parents corresponding to the year before diagnosis/reference year were obtained from the Danish Civil Registration System[12] and Statistics Denmark including: vital status, birth year, country of birth, place of residence (Copenhagen and suburbs, provincial cities, rural), education (short, medium, higher)[17], employment situation (employed, unemployed)[15], and income (lowest quintile, not lowest quintile). Education was categorized according to ISCED codes [short: early childhood education, primary education and lower secondary education (ISCED levels 0-2); medium: general upper secondary education, high school programs and vocational upper secondary education, vocational training and education (ISCED level 3); high: short-cycle tertiary general or vocational education, Bachelor's or equivalent level, Master's or equivalent level, Doctoral or equivalent level (ISCED level 4-8)]. Characteristics of the child with cancer were obtained from the Danish Cancer Registry[11] including: calendar period of diagnosis (1982-1999; 2000-2014), sex, vital status by follow-up year, age at diagnosis, and cancer type. Childhood cancer cases were classified according to the International Classification of Childhood Cancer, ICCC 1st version (Birch and Marsden Classification[18]) until 2003 and ICCC 3rd version[19] thereafter, and categorized into six main diagnostic groups: lymphoid leukemia; other leukemia; lymphoma; central nervous system (CNS) tumor, bone tumor/soft tissue sarcoma, and other solid tumor.

Statistical analysis

For the analysis of separation and divorce, the study population was restricted to parents that were either cohabiting (n=5245 case parent-couples, n=52599 comparison parent-couples) or married (n=4371 case parent-couples, n=43881 comparison parent-couples) to the respective other parent in

the year before diagnosis/reference year. Case and comparison parent-couples were followed from one year before diagnosis/reference year until 10 years after diagnosis/reference year, separation or divorce, death, emigration, or end of study (December 2017), whichever came first. For visual presentation, we plotted the proportion of separated and divorced parent-couples over the follow-up period. Taking into account that information on separation and divorce was only available annually, we fitted discrete-time Cox regression models to compare the risk of separation and divorce between case and comparison parent-couples with the follow-up period separated into one-year intervals by using the *cloglog* procedure in Stata version 14.2 (StataCorp LP, College Station, TX). Additionally to crude models, we fitted multivariate models adjusting for parental age, education, country of birth, income, and place of residence.

Among case parent-couples only, we used discrete-time Cox regression models to identify socio-demographic and cancer-related risk factors of separation and divorce. To assess the independence of associations from the univariate analysis, we fitted two multivariate models including i) all socio-demographic and ii) all cancer-related factors. As visual inspection indicated that events of separation and divorce predominantly occurred from three years after diagnosis/reference year, we restricted the follow-up period for this analysis accordingly. Results from discrete-time Cox regression were expressed as hazard ratios (HR) with two-sided 95% confidence intervals (CI).

For the analysis of family planning, we used the entire cohort of case and comparison parents irrespective of cohabitation or marital status with the other parent. Analyses were performed separately for mothers and fathers as the number of children may differ between them. We used tests for trend across ordered groups to separately compare the number of children (total, before/after index date) between case and comparison parents. Two-sided t-tests were used to compare the time to birth of next child between case and comparison parents.

Results

The distribution of socio-demographic characteristics was similar between case and comparison parents (Table 1). Case parents had a slightly reduced risk of parental separation (HR=0.96, 95%-CI: 0.93-0.99) and divorce (HR=0.92, 95%-CI: 0.87-0.97) than comparison parents (Figure 2). Effect estimates remained similar after adjusting for socio-demographic characteristics for separation (HR=0.95, 95%-CI: 0.92-0.98) and divorce (HR=0.91, 95%-CI: 0.86-0.96).

Case parents aged <45 years, with short education, and who were unemployed one year before diagnosis/reference year were at increased risk of separation and divorce compared to parents of older age, with higher education, and who were employed one year before diagnosis/reference year, respectively (Table 2). Effect sizes were higher for maternal education compared to paternal education and lower for mothers´ than fathers´ employment situation. No significant associations were identified for parents´ country of birth, place of residence, and income. The multivariate model including all socio-demographic characteristics showed overall comparable patterns with lower and less precise effect estimates (Supplemental table 1).

In terms of cancer-related characteristics, we found that parents of children diagnosed in the earlier period (1982-1999 vs. 2000-2014) were at lower risk of separation and divorce (Table 2). We further found that parents of children diagnosed with cancer at a younger age (aged <15 years) were at increased risk of separation and divorce. Similar patterns were observed in the multivariate regression model including all cancer-related characteristics (Supplementary table 2). We found elevated risks of separation (HR=1.12, 95%-CI: 1.02-1.23) and divorce (HR=1.32, 95%-CI: 1.13-1.54) among parents of children diagnosed with lymphoid leukemia compared to parents of children diagnosed with other solid tumors (Table 2), however the association disappeared when adjusting for other cancer-related characteristics including age at diagnosis (Supplementary table 2).

For the analyses of family planning, we found that case mothers were more likely to have ≥2 other children after the index date than comparison mothers (6.1% vs. 3.8%; $p_{trend}<0.001$; Table 3). Similarly, we found that case fathers more often had ≥2 other children after the index date than

comparison fathers (7.0% vs. 4.3%; $p_{trend}<0.001$). However, overall differences were small. Mean time to next birth was 1020 days (95%-CI: 974-1066) in case mothers and 978 days (95%-CI: 961-994) in comparison mothers, which was not statistically significant (p=0.101). Time to next birth was 1087 days (95%-CI: 1029-1145) in case fathers and 1117 days (95%-CI: 1093-1140) in comparison fathers (p=0.410).

Discussion

This nationwide population-based cohort of more than 135000 parents from Denmark revealed a small risk reduction of 4% for parental separation and 8% for divorce among parents of children with cancer compared to parents of cancer-free children. Among parents of children with cancer, elevated risks for separation and divorce were identified among parents of younger age, with short education, and who were unemployed. Risks were also elevated among parents of more recently diagnosed children and children diagnosed at a younger age. The childhood cancer experience did not adversely affect parents´ future family planning.

Parents of children with cancer are faced with tremendous emotional demands that may interfere with parents´ couple functioning[4]. However, two previous studies from Norway[7] and Denmark[6] found no evidence or increased divorce or separation risks. Although we observed that parents of children diagnosed more recently were at increased risk of separation and divorce compared to the earlier diagnosis period, we revealed a small overall risk reduction of 4% for parental separation and 8% for divorce compared to parents of cancer-free children. This indicates that comparison parents did undergo similar or even more pronounced changes over time which may be related to general societal changes. The impact on the relationship of parents of children with cancer may also have decreased over time due to modifications of treatment modalities towards less intensive approaches[10].

Collectively, these findings suggest that the potentially adverse effect of childhood cancer on the parents´ relationship may be outweighed by opposite contributions that may have strengthened parental bonding in many couples. There is indeed evidence suggesting that a child's disease led to a feeling of mutual commitment among some parents, and that this common experience ultimately improved the quality of their relationship[8, 20-22]. A child´s cancer diagnosis may also alter parents´ life priorities and conflicts in the parental relationship may be perceived as less important compared to the childhood cancer experience[7]. The literature further suggests that parents may also experience post-traumatic growth following their child's disease that contributes to increased family orientation and closeness[23].

We found that the risk of separation and divorce may be influenced by the socio-economic position of parents of children with cancer. Similar findings have been previously observed in parents of cancer-free children[6]. Higher economic strains have been shown to be related to worse marital adjustment in families of children with cancer[24]. Parents with lower socio-economic position may be more often engaged in less flexible work arrangements[25, 26] and burdened by combining childcare and work-related obligations which may strain the parental relationship. We further observed elevated risks of separation and divorce in parents of children diagnosed at a younger age and parents of children with lymphoid leukemia. Compared to other diagnostic groups, treatment procedures for lymphoid leukemia are more demanding as it may last for several years[27]. However, the association with lymphoid leukemia did not persist when accounting for other cancer-related characteristics and appears to be explained by the commonly young age at disease onset. Regardless of any health condition, younger children require more parental care what may be particularly burdensome in the life-threatening context of having a child with cancer[5].

To our knowledge, this is the first population-based study investigating the impact of childhood cancer on family planning. Childhood cancer requires some degree of family re-organization to accommodate the needs of the diseased child[2]. We expected that parents having a child with cancer would have fewer children compared to parents of cancer-free children and could postpone having another child. However, this was not seen in our study. Despite changes in family structures and strains, the cancer experience may also have contributed to strengthen family relationship s and to increase family orientation and prioritization[2]. In line with our findings, previous research indicated that family functioning, cohesion, and flexibility are similar between families of children with cancer and comparison samples[2]. Nevertheless, parents perceiving concerns in regard to having another child should be offered support and reassurance by the respective health care professionals.

Collectively, our findings suggest that while the family system is able to adapt to the situation throughout the child´s cancer trajectory in the majority of families. However, particularly parents of lower socio-economic position and with children diagnosed at a younger age might benefit from

additional support to improve family outcomes[28]. Currently, family support services are largely limited to the child's in-patient treatment including support by hospital staff such as social workers or psycho-oncologists as well as through community organisations. Additionally, during and after treatment, families may also have the opportunity to attend family camps, which may potentially increase family reconnection[29]. However, while more general support services such as marital counselling are widely available, cancer-specific family support services are often lacking after the child's treatment. As the child's long-term need for medical care may continue beyond cancer treatment, survivorship or late effect clinics may potentially represent a framework to integrate long-term family support.

Limitations and strengths

A major strength of our study is the nationwide register-based cohort design including a large sample of parents. The use of high-quality registry data with virtually no loss to follow-up minimizes the risk of bias. The national registries cover all children diagnosed with cancer and therefore adequately reflects the situation in Denmark. Another strength refers to our definition of the parental relationship that was not limited to the parents´ marital status but included the increasingly common cohabitation without being married. We were further able to include a broad range of socio-demographic and cancer-related covariates, including information before the child´s diagnosis. A limitation of our study refers to the lack of in-depth information on relationship satisfaction that needs to be addressed in future studies and may not necessarily be reflected in our outcomes. Moreover, our study included both parents of survivors and bereaved parents, which may have a different experience along their child's disease trajectory.

Conclusion

In conclusion, our observations from Denmark showed that having a child with cancer was not associated with an overall adverse impact on parents' risk of separation or divorce and future family planning. These overall reassuring and encouraging findings should be communicated from clinicians to parents to support them along their child´s cancer trajectory.

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Table 1. Characteristics of parents of children diagnosed with cancer in 1982-2014 (case parents) and parents of cancer-free children (comparison parents)

	Case parents (n=12418)				Comparison parents (n=125014)			
	Mothers (n=6833)		Fathers (n=5585)		Mothers (n=68773)		Fathers (n=56241)	
Socio-demographic characteristics	n	%	n	%	n	%	n	%
Age[a,b]								
<30 years	1191	17.4	565	10.1	11530	16.8	5637	10.0
30-34 years	1416	20.7	973	17.4	14405	21.0	10061	17.9
35-39 years	1628	23.8	1225	21.9	16337	23.8	12478	22.2
40-44 years	1471	21.5	1299	23.3	14726	21.4	12708	22.6
≥45 years	1127	16.5	1523	27.3	11775	17.1	15357	27.3
Education[a,c,d]								
Short	1438	21.4	1031	18.9	13908	20.6	9824	17.8
Medium	3209	47.8	2954	54.0	32403	48.0	29562	53.7
Higher	2067	30.8	1485	27.2	21222	31.4	15715	28.5
Country of birth[c]								
Denmark	6292	92.1	5091	91.2	62916	91.5	51550	91.7
Other	541	7.9	494	8.9	5856	8.5	4690	8.3
Employment situation[a,c,e]								
Unemployed	1192	16.9	368	6.6	11609	16.9	3518	6.3
Employed	5346	78.2	5079	90.9	54697	79.5	51510	91.6
Other	295	4.3	138	2.5	2467	3.6	1213	2.2
Income[a,c]								
Lowest quintile	398	5.8	376	6.7	4720	6.9	4047	7.2
Not lowest quintile	6435	94.2	5209	93.3	64052	93.1	52193	92.8
Place of residence[a,b]								
Copenhagen and suburbs	2150	31.5	1674	30.0	21050	30.6	17173	30.5
Provincial cities	2740	40.1	2219	39.7	27030	39.3	22016	39.2
Rural	1943	28.4	1692	30.3	20693	30.1	17052	30.3
Cohabitation and marital status[f]	N		%		n		%	
Cohabitation[a,b]								
No	107		2.0		1318		2.4	
Yes	5245		98.0		52599		97.6	
Marital status[a,c]								
No	957		18.0		9767		18.2	
Yes	4371		82.0		43881		81.8	
Characteristics of child with cancer	N		%		n		%	
Calendar period of diagnosis[b]								
1982-1999	3561		50.4		-		-	
2000-2014	3505		49.6		-		-	
Sex[c]								
Male	3938		55.8		-		-	
Female	3122		44.2		-		-	
Vital status[b,g]								
Alive	5236		74.1		-		-	
Deceased	1830		25.9		-		-	
Age at diagnosis[b]								
<1 year	446		6.3		-		-	
1-4 years	1364		19.3		-		-	
5-9 years	1447		20.5		-		-	
10-14 years	1230		17.4		-		-	
15-19 years	2579		36.5		-		-	
Diagnostic group[b]								
Lymphoid leukemia	1269		18.0		-		-	
Other leukemia	386		5.5		-		-	
Lymphoma	940		13.3		-		-	
CNS tumor	1776		25.1		-		-	
Bone tumor/soft tissue sarcoma	760		10.8		-		-	
Other solid tumor	1935		27.4		-		-	

[a]Characteristic assessed one year before diagnosis/reference year. [b]No missing values. [c]Missing values of <5%. [d]Education was categorized according to ISCED codes [short: early childhood education, primary education and lower secondary education (ISCED levels 0-2); medium: general upper secondary education, high school programs and vocational upper secondary education, vocational training and education (ISCED level 3); high: short-cycle tertiary general or vocational education, Bachelor's or equivalent level, Master's or equivalent level, Doctoral or equivalent level (ISCED level 4-8)]. [e] Employment situation was categorized into employed and unemployed (registered as unemployed or out of workforce). Retired parents and

parents in education were categorized as “other”. [f]Restricted to parents where the mother and father were included in the study. For marital status, only parents with the same marital status were included. [g]Refers to entire follow-up period.

Table 2. Socio-demographic and cancer-related risk factors of separation and divorce in case parents from univariate discrete-time Cox regression models

	Case parents			
	Separation (n=5245 case parent-couples)		Divorce (n=4371 case parent-couples)	
Determinant	HR[a]	95%-CI	HR[a]	95%-CI
Socio-demographic characteristics of parents[b]				
Mothers´ age				
<30 years	2.64	2.32-3.00	2.37	1.95-2.88
30-34 years	2.06	1.81-2.34	1.87	1.55-2.25
35-39 years	1.66	1.45-1.89	1.36	1.12-1.64
40-44 years	1.37	1.19-1.58	1.17	0.96-1.43
≥45 years	ref		ref	
Fathers´ age				
<30 years	2.31	2.06-2.58	1.96	1.59-2.42
30-34 years	2.07	1.87-2.29	2.21	1.89-2.59
35-39 years	1.44	1.30-1.60	1.58	1.35-1.85
40-44 years	1.15	1.03-1.28	1.06	0.89-1.25
≥45 years	ref		ref	
Mothers´ education				
Short	1.38	1.26-1.52	1.19	1.02-1.39
Medium	1.21	1.12-1.31	1.22	1.08-1.39
Higher	ref		ref	
Fathers´ education				
Short	1.39	1.26-1.53	1.07	0.91-1.26
Medium	1.08	1.00-1.18	1.03	0.90-1.17
Higher	ref		ref	
Mothers´ country of birth				
Denmark	ref		ref	
Other	0.86	0.75-0.99	0.89	0.72-1.10
Fathers´ country of birth				
Denmark	ref		ref	
Other	1.03	0.90-1.16	0.98	0.81-1.19
Mothers´ employment situation				
Unemployed	1.36	1.25-1.47	1.19	1.03-1.37
Employed	ref		ref	
Other	1.63	1.39-1.92	1.38	1.04-1.83
Fathers´ employment situation				
Unemployed	1.51	1.34-1.70	1.24	1.01-1.53
Employed	ref		ref	
Other	0.82	0.83-1.06	0.41	0.23-0.72
Mothers´ income				
Lowest quintile	1.01	0.89-1.14	0.85	0.69-1.06
Not lowest quintile	ref		ref	
Fathers´ income				
Lowest quintile	1.15	1.02-1.31	1.17	0.95-1.43
Not lowest quintile	ref		ref	
Mothers´ place of residence[c]				
Copenhagen and suburbs	ref		ref	
Provincial cities	1.00	0.92-1.08	1.05	0.92-1.20
Rural	0.92	0.84-1.00	1.07	0.93-1.22
Fathers´ place of residence[c]				
Copenhagen and suburbs	ref		ref	
Provincial cities	1.00	0.92-1.08	1.06	0.93-1.21
Rural	0.92	0.84-1.00	1.06	0.93-1.22
Characteristics of the child with cancer				
Calendar period of diagnosis				
1982-1999	0.80	0.75-0.85	0.64	0.58-0.71
2000-2014	ref		ref	
Gender				

Male	ref		ref	
Female	0.99	0.92-1.05	0.95	0.86-1.06

Table 2. Continued

	Case parents			
	Separation (n=5245 case parent-couples)		Divorce (n=4371 case parent-couples)	
Determinant	HR[a]	95%-CI	HR[a]	95%-CI
Vital status[e]				
Alive	ref		ref	
Deceased	1.01	0.94-1.09	0.88	0.78-0.99
Age at diagnosis				
<1 year	1.74	1.52-1.98	1.07	0.78-1.45
1-4 years	1.77	1.62-1.94	1.61	1.39-1.87
5-9 years	1.54	1.40-1.70	1.85	1.61-2.13
10-14 years	1.24	1.11-1.37	1.21	1.03-1.43
15-19 years	ref		ref	
Diagnostic group				
Lymphoid leukemia	1.12	1.02-1.23	1.32	1.13-1.54
Other leukemia	1.06	0.91-1.23	1.62	1.30-2.01
Lymphoma	0.79	0.69-0.89	0.90	0.74-1.09
CNS tumor	1.06	0.97-1.16	0.88	0.76-1.03
Bone tumor/soft tissue sarcoma	0.91	0.80-1.03	0.99	0.82-1.20
Other solid tumor	ref		ref	

CI, confidence interval; CNS, central nervous system; HR, hazard ratio; n.a., not applicable.

[a]HR>1 indicate higher likelihood of separation and divorce; HR<1 indicate lower likelihood of separation and divorce. [b]Socio-demographic characteristics assessed one year before diagnosis. [c]Identical effect estimates for mothers and fathers for the outcome separation as they were cohabiting one year before diagnosis/reference year. [e]Refers to entire follow-up period.

Table 3. Analysis of family planning: number of children

	Mothers (n=75606)					Fathers (n=61826)				
	Case mothers (n=6833)		Comparison mothers (n=68773)			Case fathers (n=5585)		Comparison fathers (n=56241)		
	n	%	n	%	P-value	n	%	n	%	P-value
Total number of children[a]					0.275					<0.001
No other child	551	8.1	4473	6.5		331	5.9	3833	6.8	
1 other child	3132	45.8	33758	49.1		2512	45.0	26420	47.0	
≥2 other children	3150	46.1	30542	44.4		2742	49.1	58988	46.2	
Number of children before index date[a,b]					<0.001					0.801
No other child	1133	16.6	9653	14.0		798	14.3	8226	14.6	
1 other child	3326	48.7	34211	49.7		2721	48.7	26948	47.9	
≥2 other children	2374	34.7	24909	36.2		2066	37.0	21067	37.5	
Number of children after index date[a,b]					<0.001					<0.001
No other child	5506	80.6	57754	84.0		4412	79.0	46549	82.8	
1 other child	910	13.3	8426	12.3		784	14.0	7263	12.9	
≥2 other children	417	6.1	2593	3.8		389	7.0	2429	4.3	

SD, standard deviation.

[a]Index child not included. [b]Index date refers to diagnosis date among case parents and respective reference date in comparison parents.

Figure 1. Flow chart of study population

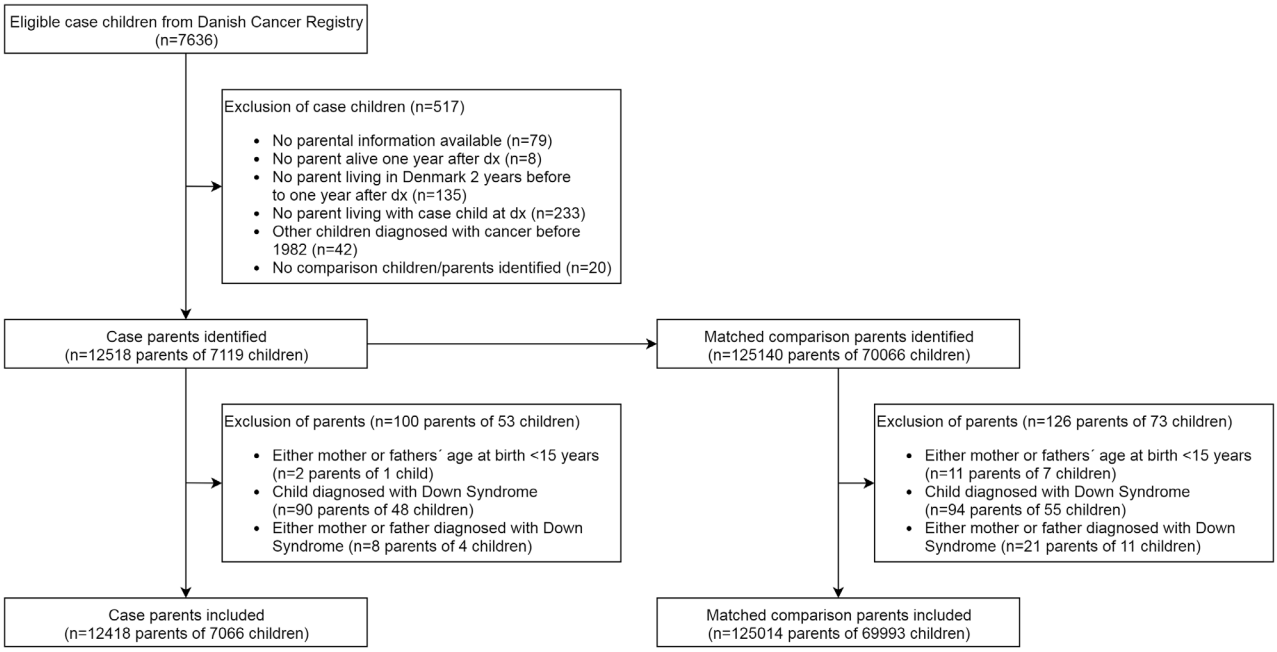
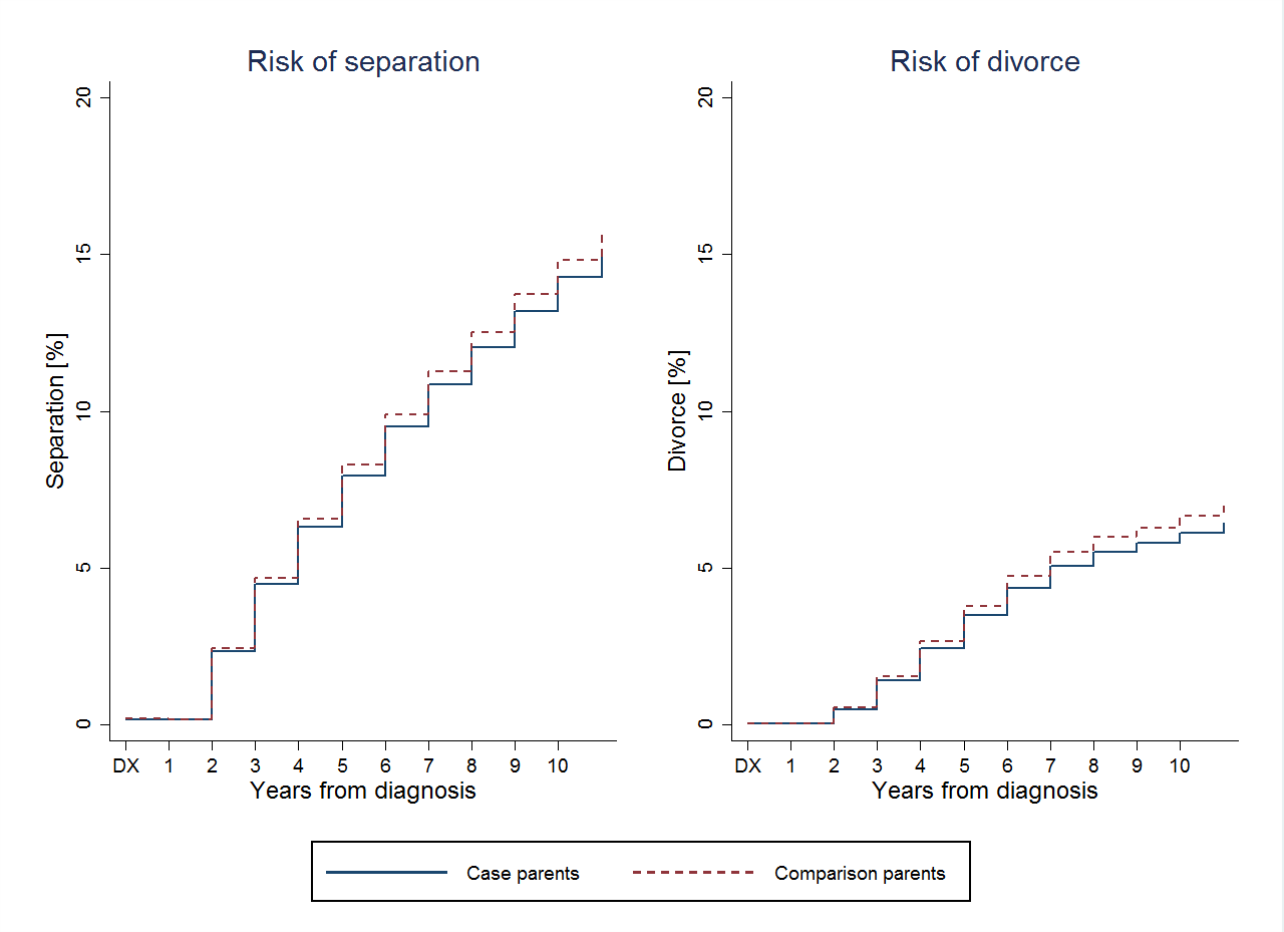


Figure 2. The risk of separation and divorce in case and comparison parents during the follow-up period



Supplementary material. Detailed description of cohort definition and matching criteria

The study population was defined by parents of children diagnosed with cancer and matched population-based comparison parents of cancer-free children. The selection and definition of our study population was performed in a 3-step-procedure (see also Figure 1):

1) Identification of children diagnosed with cancer and their parents:

Based on information from the Danish Cancer Registry, case children were eligible if they fulfilled the following inclusion criteria:

- First, primary cancer diagnosis before the age of 20 years
- Diagnosed in the period from 1982-2014

The children's unique identification number allowed linkage to their (biological and adoptive) parents via the Danish Medical Birth Register and the Civil Registration System. Among the 7636 children meeting the inclusion criteria as specified above, we applied the following exclusion criteria based on their parents:

- No parental information available (n=79)
- No parent alive one year after diagnosis (n=8)
- No parent living in Denmark 2 years before to one year after diagnosis (n=135)
- No parent living with child at diagnosis (n=233)
- Parents had other children diagnosed with cancer before 1982 (n=42)
- Lack of information to identify comparison children/parents (n=20)

This resulted in a sample of 7119 case children with sufficient information to identify the respective parents (n=12518).

2) Identification and matching of comparison parents:

Comparison parents were restricted to parents of children without any cancer diagnosis during the entire follow-up period that were alive and living in Denmark in the respective reference year. Cancer-free children were required to live with at least one parent in the reference year. Ten comparison parents per case parent were randomly sampled (sampling with replacement) from the entire Danish population by using the following matching variables based on information from the Civil Registration System:

- Child's year of birth
- Mother's decade of birth
- Father's decade of birth

If both parents were available, all matching factors were applied. If only the mother or father was available, only mother's or father's decade of birth was used. The matching ratio of 1:10 was chosen in order to increase statistical power. The main rationale for selecting only basic age-related variables was to avoid overmatching for potential mediators in later outcome analysis. As a result of the matching procedure, we identified 125140 comparison parents of 70066 cancer-free children.

3) Exclusion of ineligible case and comparison parents:

Among both case and comparison parents, we further applied the following exclusion criteria:

- Diagnosis of Down Syndrome in either child or parent
- Parental age at child's birth <15 years

The final study cohort included 12418 case parents (n=6833 mothers, n=5585 fathers) and 125014 comparison parents (n=68773 mothers, n=56241 fathers). For the analysis of separation and divorce, the study population was further restricted to parents that were either cohabiting (n=5245 case parent-

couples, n=52599 comparison parent-couples) or married (n=4371 case parent-couples, n=43881 comparison parent-couples) to the respective other parent in the year before diagnosis/reference year.

Supplementary table 1. Socio-demographic risk factors of separation and divorce in case parents from multivariate discrete-time Cox regression models

	Case parents			
	Separation[a] (n=5245 case parent-couples)		Divorce[b] (n=4371 case parent-couples)	
Determinant	HR[c]	95%-CI	HR[c]	95%-CI
Socio-demographic characteristics of parents[d]				
Mothers´ age				
<30 years	1.60	1-30-1.97	1.57	1.13-2.17
30-34 years	1.55	1.28-1.87	1.28	0.96-1.71
35-39 years	1.55	1.30-1.83	1.13	0.88-1.47
40-44 years	1.28	1.10-1.49	1.10	0.88-1.38
≥45 years	ref		ref	
Fathers´ age				
<30 years	1.56	1.29-1.89	1.22	0.88-1.71
30-34 years	1.48	1.25-1.75	1.68	1.29-2.20
35-39 years	1.06	0.92-1.24	1.34	1.06-1.70
40-44 years	0.95	0.83-1.09	1.00	0.82-1.22
≥45 years	ref		ref	
Mothers´ education				
Short	1.18	1.05-1.31	1.21	1.01-1.45
Medium	1.12	1.02-1.22	1.21	1.06-1.40
Higher	ref		ref	
Fathers´ education				
Short	1.23	1.11-1.38	0.94	0.79-1.13
Medium	0.96	0.88-1.05	0.89	0.77-1.03
Higher	ref		ref	
Mothers´ country of birth				
Denmark	ref		ref	
Other	0.58	0.47-0.72	0.78	0.57-1.06
Fathers´ country of birth				
Denmark	ref		ref	
Other	1.13	0.94-1.35	1.16	0.87-1.54
Mothers´ employment situation				
Unemployed	1.14	1.03-1.25	1.08	0.91-1.28
Employed	ref		ref	
Other	1.55	1.30-1.84	1.50	1.12-2.01
Fathers´ employment situation				
Unemployed	1.27	1.11-1.46	1.12	0.88-1.42
Employed	ref		ref	
Other	1.55	1.30-1.84	0.54	0.30-0.96
Mothers´ income				
Lowest quintile	0.90	0.78-1.04	0.80	0.63-1.02
Not lowest quintile	ref		ref	
Fathers´ income				
Lowest quintile	1.12	0.98-1.27	1.13	0.92-1.40
Not lowest quintile	ref		ref	
Mothers´ place of residence[e]				
Copenhagen and suburbs	ref		ref	
Provincial cities	0.94	0.86-1.02	0.22	0.05-0.95
Rural	0.85	0.77-0.92	3.81	0.88-16.5
Fathers´ place of residence[e]				
Copenhagen and suburbs	ref		ref	
Provincial cities	0.94	0.86-1.02	4.63	1.07-20.07
Rural	0.85	0.77-0.92	0.27	0.06-1.15

CI, confidence interval; CNS, central nervous system; HR, hazard ratio; n.a., not applicable.

[a]Analysis of separation restricted to case parents that were cohabiting one year before diagnosis (n=5245 case parent-couples). [b]Analysis of divorce restricted to case parents that were registered as married one year before diagnosis (n=4371 case parent-couples). [c]Hazard ratios from multivariabe discrete-time Cox regression model including all socio-demographic characteristics of parents with the underlying time scale starting in year three after

diagnosis: HR>1 indicate higher likelihood of separation and divorce; HR<1 indicate lower likelihood of separation and divorce. [d]Socio-demographic characteristics of parents assessed one year before diagnosis. [e]Identical effect estimates for mothers and fathers for the outcome separation as they were cohabiting one year before diagnosis/reference year.

Supplementary table 2. Cancer-related risk factors of separation and divorce in case parents from multivariate discrete-time Cox regression models

	Case parents			
	Separation[a] (n=5245 case parent-couples)		Divorce[b] (n=4371 case parent-couples)	
Determinant	HR[c]	95%-CI	HR[c]	95%-CI
Characteristics of the child with cancer				
Calendar period of diagnosis				
1982-1999	0.80	0.75-0.85	0.65	0.58-0.72
2000-2014	ref		ref	
Gender				
Male	ref		ref	
Female	0.96	0.90-1.02	0.92	0.83-1.02
Vital status[d]				
Alive	ref		ref	
Deceased	1.05	0.97-1.13	0.95	0.84-1.08
Age at diagnosis				
<1 year	1.69	1.48-1.94	1.03	0.76-1.41
1-4 years	1.73	1.57-1.91	1.54	1.31-1.80
5-9 years	1.52	1.38-1.68	1.87	1.62-2.17
10-14 years	1.23	1.10-1.36	1.24	1.05-1.46
15-19 years	ref		ref	
Diagnostic group				
Lymphoid leukaemia	0.99	0.89-1.09	1.07	0.91-1.25
Other leukaemia	1.01	0.86-1.17	1.59	1.28-1.98
Lymphoma	0.89	0.78-1.01	0.92	0.75-1.11
CNS tumour	1.04	0.95-1.14	0.81	0.69-0.94
Bone tumour/soft tissue sarcoma	0.95	0.84-1.07	0.97	0.79-1.18
Other solid tumour	ref		ref	

CI, confidence interval; CNS, central nervous system; HR, hazard ratio; n.a., not applicable.

[a]Analysis of separation restricted to case parents that were cohabiting one year before diagnosis (n=5245 case parent-couples).

[b]Analysis of divorce restricted to case parents that were registered as married one year before diagnosis (n=4371 case parent-couples).

[c]Hazard ratios from multivariabe discrete-time Cox regression model including all cancer-related characteristics with the underlying time scale starting in year three after diagnosis: HR>1 indicate higher likelihood of separation and divorce; HR<1 indicate lower likelihood of separation and divorce.

[d]Refers to entire follow-up period.